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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,228	06/29/2005	Keiji Hasumi	05360/HG	4548

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FRISHAUF, HOLTZ, GOODMAN & CHICK, PC
220 Fifth Avenue
16TH Floor
NEW YORK, NY 10001-7708

EXAMINER	
KOSAR, AARON J	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,228	HASUMI ET AL.	
	Examiner	Art Unit	
	Aaron J. Kosar	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/29/05; 9/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and argument filed September 26, 2007 in response to the non-final rejection are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Applicant's election of species:(a) bacillolysin MA (BL-MA), (b) agarose, (c) Lys, and (d) plasminogen, in the reply filed on December 18, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant has amended the claims by amending the claims, including introducing new claims 5-14.

Claims 1-14 are pending. Claims 10 and 11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. **Claims 1-9 and 12-14** are pending and have been examined on their merits to the extent the claims are drawn to the elected species.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on September 26, 2007, was filed after the mailing date of the Office Action (non-final rejection) on May 30, 2007. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the Examiner, and has been placed in the application file.

Also the references of SHIMIZU and of HASUMI were not considered (i.e. lined-through) in the Office Action of May 30, 2007 for the reasons of record, and were submitted, but

not listed on the IDS of September 26, 2007; however, these foreign language non-patent literature documents have been provided and *have been considered* herein to the extent as evidenced by the portions provided in English language text, provided in the equivalent translation or representative figures, disclosed by the instant specification or by an international search report (ISR), or as made of record/argued in the instant Office Action. As such, the IDS and accompanying references of Shimizu and Hasumi have been placed in the Application file. Arguments to Shimizu and Hasumi have been considered as prompted by the submission of an IDS, though for the sake of compact prosecution, their citations have been listed on a PTO-892.

Additionally, courtesy copies of each signed IDS (5/30/05, 9/26/07) is provided herewith. The Examiner has indicated an extent for which JP 2002-272453 was considered and Applicant has also asserted the inclusion of the ISR and page 1 of the instant specification as further evidence. In this regard, the Examiner agrees with Applicant's assertion. Also please note, this additional extent though not itemized by the Examiner is implicit in the art and/or documents of record in the instant Application; and, as such, the Examiner asserts JP 2002-272453 *has been considered* (signed copy of IDS, 6/29/2005; see also 37 CFR § 1.98).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The claims are generally drawn to an assembly of components into a molecule-support-enzyme composition. The dependent claims are drawn to species of components, including

species of molecule, Lysine; support, agarose-based compositions; and enzyme, bacillolysin MA and other enzyme species.

(Maintained) Claims 1-3, 5-9, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by MCCLUNG (McClung, W.G., et al. Journal of Biomedical Materials Research. 2000,49(3), 409-414) or RÖMISCH (U.S. Patent 6,528,299) or FISCHER (U.S. Patent 6,228,613).

MCCLUNG anticipates the claims by motivating tPA binding to a surface through lysine moieties, the binding of plasminogen to lysine, and the conversion of plasminogen to plasmin via a plasminogen/plasmin complex bound to a lysine-rich support surface (McClung, conclusion, page 414).

RÖMISCH teaches a chromatographic system that employs a substrate that immobilizes heparin/heparin-related compounds. These compounds also bind to protease and/or proenzyme giving the compounds dual status as both the linker and the enzyme's substrate (Römisch, column 2, ¶4).

FISCHER teaches an organizational interrelationship of the components similar to Römisch, Fischer describing a chromatographic system that uses a heparin affinity chromatography (substrate, lysine; support, Sepharose) to selectively bind to plasma protease (Fischer, column 16, Example 7).

Response to arguments

Applicant has argued that the prior art reactors lack an enzyme and a molecule that specifically and directly bind to a substrate of the enzyme and that the intended use of the reactors of McClung/Römisch/Fischer are for protease elution, not enzymatic action on the

enzyme's substrate. This is not found to be persuasive, however, because the reactors of McClung/Römisch/Fischer, when the components are bound directly or indirectly and thus "immobilized" to the protease/proenzyme, are still determined to anticipate the claims to the extent of the reactor composition, especially in the absence of evidence as to the criticality, or objective evidence to the contrary, or a chemical structure unambiguously defining the nature of the immobilization interaction. Also, to the extent that McClung/Römisch/Fischer may differ regarding select combinations or elected species, McClung/Römisch/Fischer are still deemed to anticipate the claims as evidence of the non-allowability of the generic claims/invention.

(New) Claims 1-3, 5-9, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by SHIMIZU ((**U-1:**PTO-892) Kosuke Shimizu, Ritsuko Narasaki, Harushige Kuribayashi, Tsutomu Sato, and Keiji Hasumi. "One step purification of angiostatin from plasma using a new processing protease bacillolysin MA" Journal of Biochemistry. August 2002, 74(8), 4P-459 (English Translation) and supplemental figures.)

SHIMIZU teaches a one-step process of angiostatin conversion and purification from plasma/plasminogen using the protease bacillolysin-MA (BLMA) fixed to a carrier and also lysine bound to the carrier (see Shimizu: title; purpose; method and results). Although the teachings of Shimizu *on page 4P-459* is silent regarding the nature of the interaction of the lysine or the enzyme with a particular substrate, said interaction would be intrinsic properties of the compounds. Furthermore, as Shimizu teaches a composition having the same elements, in the same combination, and for the same purpose (e.g. one-step production of angiostatin from plasminogen in a plasma sample) as the instant claims, absent evidence to the contrary or

evidence to the criticality of some undisclosed and unexpected structural-functional relationship of such a composition, the composition of Shimizu and that of the instant claims would be expected to have the same properties.

Additionally, Shimizu (including the supplemental figures/panels 1-10) teaches the composition of a BL/Sepharose support linked to lysine and also linked to BL-MA (e.g. see panels 7 and 9 teaching "BL/Lys-Sepharose" the analogous structure having lysine additionally bound to plasminogen) and a one step method of converting plasminogen to the BL-MA cleaved product and the temperature of 4 ºC (e.g. panels "8" and "9").

(New) Claims 1-9, and 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by HASUMI ((**V-1**: PTO-892) Keiji Hasumi, "A New Microbiological Enzyme which Catalyzes Angiostatin Conversion of Plasminogen," Mishima Kaiun Memorial Foundation, Research Report, NO. 39, (2001), pages 60-64 (English abstract and portions of text in the English language))

HASUMI (**V-1:**PTO-892) anticipates the claims by teaching a fixed-enzyme composition in a one-step purification of plasma to form angiostatin (English abstract). Hasumi also teaches the coupling of a lysine-agarose-based support, lysine-SEPHAROSE®, to bacillolysin "MA" from the organism *Bacillus meaterium* A9542 (right column, page 60) using CNBr to produce the "fixed" compositions 5-,16-, 30- and BL/Lys-SEPHAROSE® and using isopropanol at 4ºC (e.g. page 61, (synthesis of BL-Lys-Sephaorse: 3(1),3(2), and method of using: 4, page 61; table/figure 1, page 62; abstract) for this angiostatin conversion process.

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on September 26, 2007 and Applicant's amendment prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aaron J. Kosar whose telephone number is (571) 270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday,EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Aaron Kosar/
Examiner, Art Unit 1651

/Sandra Saucier/
Primary Examiner, Art Unit 1651